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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
FERNANDEZ, SUSAN EMILY	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 04/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/804,800	MARKOV ET AL.	
	Examiner	Art Unit	
	Susan E. Fernandez	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *March 22, 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-82* is/are pending in the application.

4a) Of the above claim(s) *62-82* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/25/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-82 are pending and are presented for examination.

Election/Restrictions

Applicant's election with traverse of the group I invention, claims 1-30 in the reply filed on March 22, 2005, is acknowledged. The traversal is on the ground(s) that the methods defined by claims 31-61 are species of the method defined by generic claim 1. In view of the arguments presented, the restriction requirement between groups I and II is hereby withdrawn.

The requirement between group III and the other restriction groups is still deemed proper and is therefore made FINAL.

Claims 62-82 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on March 22, 2005.

Claims 1-61 are examined on the merits to the extent they read on the elected subject matter.

Information Disclosure Statement

The information disclosure statement filed February 25, 2002, fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information

or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-61 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rendered indefinite by the phrase, "biological window of a magnetic field". It is not clear what constitutes the "biological window of a magnetic field". Furthermore, the terms "MLC" and "MLCK" render claim 1 indefinite because they are never defined in the claims. These terms should be defined the first instance they appear in the claims. Thus claims 1-30 are rejected under 35 U.S.C. 112, second paragraph.

Various claims are indefinite because they describe steps which include steps ("the method of...wherein the step...includes the following step"). It is not clear how a step can include a step. Thus claims 5-13, 15-19, 21-22, 24-30, 37-43, 45-49, 51-52, and 54-61 are rejected under 35 U.S.C. 112, second paragraph.

The term, "TCA", renders claim 9 indefinite because it is never defined in the claims. This term should be defined the first instance it appears in the claims. Thus claim 9 is rejected under 35 U.S.C. 112, second paragraph.

Claim 12 is indefinite because it is not clear how the phrase before the colon is related to the phrase following the colon. Thus claim 12 is rejected under 35 U.S.C. 112, second paragraph.

Claim 30 is indefinite because it consists of a grammatical error. Specifically, the phrase, "exposure such further includes...", is unclear. Thus claim 30 is rejected under 35 U.S.C. 112, second paragraph.

Claim 31 is rendered indefinite by the phrase, "relative biological effectiveness of a magnetic field". It is not clear what constitutes the "biological window of a magnetic field". In particular, it is unclear what characteristics would be used to judge the biological effectiveness of a magnetic field. Thus claims 31-61 are rejected under 35 U.S.C. 112, second paragraph.

Claim 42 is indefinite because it is not clear how the phrase preceding the colon is related to the phrase following the colon. Thus claim 42 is rejected under 35 U.S.C. 112, second paragraph.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-13, 31-43, and 61 are rejected under 35 U.S.C. 102(a) as being anticipated by Coulton et al. (Bioelectromagnetics, 2000, 21(3): 189-196).

Coulton et al. discloses a myosin light chain kinase (MLCK) assay wherein a reaction mixture is prepared comprising myosin light chain (MLC), MLCK, calmodulin, [γ-^{32}P] ATP, and calcium chloride (source of free calcium ions). See "Series 2" on pages 191-192. The reaction mixture is prepared in several tubes, each of which proceed through the following steps. Each reaction mixture to exposed to magnetic fields for 5 minutes, which is within the linear portion of the time dependence curve of myosin phosphorylation rate. A stopping solution is added to each reaction mixture in order to stop the reaction. Moreover, specimen are prepared by removing aliquots and placing them on filter paper, and in doing so the effect of the magnetic field is eliminated. Then, the specimen are washed with trichloroacetic acid (TCA), an acidic solvent which is stirred. Finally, the washed specimen are placed in scintillation vials containing water which are used for Cherenkov emission measurements. Various magnetic fields are used, allowing for comparison of radioactive events associated with the specimen, as demonstrated in Figures 1-3 (pages 192-193). A holding of anticipation is clearly required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Coulton et al.

Coulton et al. discloses a MLCK assay wherein a reaction mixture is prepared comprising MLC, MLCK, calmodulin, [γ-^{32}P] ATP, and calcium chloride (source of free calcium ions). See "Series 2" on pages 191-192. The reaction mixture is prepared in several tubes, each of which proceed through the following steps. Each reaction mixture to exposed to magnetic fields for 5 minutes, which is within the linear portion of the time dependence curve of myosin phosphorylation rate. A stopping solution is added to each reaction mixture in order to stop the reaction. Moreover, specimen are prepared by removing aliquots and placing them on filter paper, and in doing so the effect of the magnetic field is eliminated. Then, the specimen are washed with trichloroacetic acid (TCA), an acidic solvent which is stirred. Finally, the washed specimen are placed in scintillation vials containing water which are used for Cherenkov emission measurements. Various magnetic fields are used, allowing for comparison of radioactive events associated with the specimen, as demonstrated in Figures 1-3 (pages 192-193).

Coulton et al. does not expressly disclose the magnetic field frequencies as required by claims 14-22 and 44-52, or the magnetic field amplitudes as required by claims 23-30 and 53-60.

The selection of suitable magnetic field frequencies and amplitudes for the assays would have been a routine matter of optimization on the part of the artisan of ordinary skill, said artisan

recognizing that the result or effect of the magnetic field on MLC phosphorylation would differ depending on the magnetic field frequencies and amplitudes employed. A holding of obviousness is clearly required.

Claims 1-3, 5-7, 13, 31-33, 35-37, 43, and 61 rejected under 35 U.S.C. 103(a) as being unpatentable over Pilla et al. (U.S. Pat. 5,723,001) in view of Bauer (U.S. Pat. 5,030,631).

Pilla et al. discloses a method for determining the effects of magnetic fields on calcium-calmodulin dependent myosin phosphorylation. See column 8, lines 15-65. The reaction mixture comprises of MLC and MLCK derived from turkey gizzard, calmodulin, and calcium chloride, wherein ^{32}P ATP is added in order to start the reaction (column 8, lines 37-44, 53-55). The reaction mixture was exposed to a magnetic field (column 8, lines 50-53), and the reaction was stopped by the addition of a LSB stopping solution. The reaction is allowed to run for 6 minutes (column 8, lines 58-59), which is within the linear portion of the time dependence curve of myosin phosphorylation rate. The number of radioactive events is determined by counting gamma ^{32}P incorporation using Cherenkov emissions (column 8, lines 55-57). In addition, two reaction solution volumes are run through the above experiment, as indicated in column 8, lines 62-65. Comparison of the radioactive events is shown on the table on column 9, lines 1-9.

Pilla et al. does not expressly disclose forming a specimen by placing a quantity of the solution exposed to the magnetic field onto a substrate, followed by washing the specimen and placing the washed specimen in a suspension liquid.

Bauer discloses an assay for MLCK activity wherein a reaction mixture is prepared consisting of MLCK, a fragment of myosin light chain, [γ-^{32}P] ATP, calmodulin, and free calcium (column 24, lines 27-42). The reaction is initiated by the addition of the ATP to the

other reaction mixture components, and the reaction is stopped by addition of HCl (column 24, lines 44-46). Once the reaction is stopped, a specimen is formed by spotting an aliquot of the reaction mixture on phosphocellulose filter paper (column 24, lines 46-49). Moreover, the specimen is washed, and then the radioactive events are counted. Because there is no mention that the specimen is removed from the washing solution, the washing solution is considered the specimen's suspension liquid.

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to have modified the steps in the Pilla invention to include the specimen preparation steps for radioactivity counting described by Bauer.

One of ordinary skill in the art would have been motivated to do this because it would have ensured that unreacted radiolabeled ATP and its radiolabeled metabolites are not included in the Cherenkov radiation measurements. Furthermore, one of ordinary skill in the art would have been motivated to make this substitution in order to assay kinase activity as suggested by the reference with a reasonable expectation of success. A holding of obviousness is clearly required.

Claims 1-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pilla et al. and Bauer as applied to claims 1-3, 5-7, 13, 31-33, 35-37, 43, and 61 above, and further in view of Hidaka et al. (U.S. Pat. 4,943,581).

As discussed above, Pilla et al. and Bauer render claims 1-3, 5-7, 13, 31-33, 35-37, 43, and 61 obvious.

These references do not expressly disclose placing the washed specimen in a container containing agitated acidic solvent, TCA, or a suspension of water. Furthermore, it does not teach the magnetic field exposure time as required by claims 4 and 34, the magnetic field frequencies as required by claims 14-22 and 44-52, or the magnetic field amplitudes as required by claims 23-30 and 53-60.

Hidaka et al. teaches an MLCK assay wherein the reaction mixture comprises of MLC, MLCK, calcium chloride, calmodulin, and [γ-^{32}P] ATP (column 4, lines 33-44). The reaction is stopped by the addition of TCA, which is an acidic solvent. Following the addition of more TCA and albumin solution, the resulting solution is centrifuged which allows for solution agitation. The precipitated protein is washed further by dissolving the protein in sodium hydroxide. Next, the precipitated protein is placed in a vial containing water, which is then used in a liquid scintillation counter where Cherenkov emission is measured. See column 4, lines 52-55.

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to have used TCA instead of LSB as the stopping solution and have agitated the stopping solution when practicing the Pilla invention. Furthermore, it would have been obvious to have suspended the washed specimen in water for use in a liquid scintillation counter. Finally, the selection of suitable magnetic field exposure times, frequencies, and amplitudes for the assays would have been a routine matter of optimization on the part of the artisan of ordinary skill, said artisan recognizing that the result or effect of the magnetic field on MLC phosphorylation would differ depending on the magnetic field exposure times, frequencies, and amplitudes employed.

One of ordinary skill in the art would have been motivated to have used agitated TCA as the stopping solution since this substitution in order to obtain a suitable method for assaying MLCK activity as suggested by the reference would have had a reasonable expectation of success. Agitation of the TCA would have ensured that the reaction is completely halted. Likewise, there would have been a reasonable expectation of success in placing the washed specimen in a vial of water for use in a liquid scintillation counter as suggested in Hidaka et al. Thus a holding of obviousness is clearly required.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan E. Fernandez whose telephone number is (571) 272-3444. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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